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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/040,103	03/17/1998	JAMES M. MASON	52494-21	1415

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EXAMINER	
GUZO, DAVID	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 02/26/2003

29

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/040,103	MASON, JAMES M.	
	Examiner	Art Unit	
	David Guzo	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6,8-11,13-19,22-40,42-65 and 68-70* is/are pending in the application.

4a) Of the above claim(s) *22-35,39 and 40* is/are withdrawn from consideration.

5)☒ Claim(s) *1,46 and 48* is/are allowed.

6)☒ Claim(s) *4,5,10,14,15,19,36-38,42-45,47,49,50,52,55,57,59,60,65 and 68-70* is/are rejected.

7)☒ Claim(s) *3, 6, 8-9, 11, 13, 16-18, 51, 53-54, 56, 58, 61-64* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 3/17/98 is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Application/Control Number: 09/040,103

Art Unit: 1636

Detailed Action

Claims 22-35 and 39-40 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 68-70 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants claim a method for transferring a heterologous gene into a human cell and also specifically claim methods wherein the human cell can be in a human or human brain, said method comprising implanting human serum resistant non-primate producer cells capable of producing human serum resistant recombinant retroviral vectors in the human. The only use, disclosed in the instant specification, for transferring a heterologous gene into human cells in any

context (i.e. *ex vivo* or *in vivo*) or by implanting the instantly disclosed retroviral vectors into humans is for the purpose of gene therapy. The claims will therefore be read as methods of gene therapy.

The test of enablement is whether one skilled in the art can make an use the claimed invention from the teachings of the application coupled with the teachings of the prior art without undue experimentation (*United States v. Telectronics Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988). Whether undue experimentation is needed is not based upon a single factor but rather is a conclusion reached by weighing many factors (See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and *In re Wands*, 8 USPQ2d 1400 (Fed. Cir, 1988). These factors include the following:

1) Unpredictability of the art. The gene therapy art is highly unpredictable. The unpredictability is manifested in virtually all aspects of gene therapy. The primary areas of unpredictability involve delivery of the vectors to the appropriate tissues, targeting of the vectors to the appropriate cells, the transient and unpredictable expression of the transgene in cells in vivo and the lack of suitable animal models of human diseases where results of potential gene therapy treatments can be extrapolated to humans. Specifically, with regard to retroviral vectors, additional problems exist with regard to random integration into the cellular genome with the associated possible disruption of normal genes, activation of oncogenes, etc. Indeed, at present

all U.S. clinical studies using retroviruses as gene therapy agents are on hold due to the possibility that retroviral vectors may result in leukemia in patients treated with the vectors (See Marshall, Science, 2003, Vol. 299, No. 5605, p. 320). For reviews of the unpredictability of gene therapy techniques, see Mountain, TIBTECH, 2000, Vol. 18, pp. 119-128; Kmiec, American Scientist, 1999, Vol. 87, pp. 240-247; Anderson, Nature, 1998, Vol. 392, pp. 25-30; Verma et al., Nature, 1997, Vol. 389, pp. 239-242; Paillard, Human Gene Therapy, 1998, Vol. 9, pp. 767-768; Fox, Nature Biotechnology, 2000, Vol. 18, pp. 143-144, etc.

2) State of the art. At the time of filing of the instant application, no successful gene therapy protocols had been unambiguously demonstrated to be successful.

3) Number of working examples. Applicants present no working examples of the claimed invention.

4) Amount of guidance presented by applicants. Applicants present generic guidance on administering the retroviral vector producing cells to animals or humans. Applicants however present no guidance on how the skilled artisan would overcome the art recognized problems associated with successful practicing of gene therapy using retroviral vectors.

5) Nature of the invention. The invention involves one of the most complex and unpredictable areas of molecular biology/medicine; the use of viral gene therapy vectors to treat disease in humans.

6) Level of skill in the art. The level of skill in the art is high; however, given the unpredictable nature of the art, the poorly developed state of the art, the lack of guidance provided by applicants and lack of working examples, the skilled artisan would have needed to have conducted trial and error experimentation in order to practice the claimed invention.

Given the above analysis of the factors which the courts have determined are critical in determining whether a claimed invention is enabled, it must be considered that the skilled artisan would have needed to conduct undue and excessive experimentation in order to practice the claimed invention.

Claims 4, 10, 14, 15, 19, 36-38, 42-45, 47, 49, 50, 52, 55, 57, 59, 60, 65, 68-70 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants claim methods of preparing stable retroviral producer cell lines (from the cell line Mpf) for the generation of human serum resistant retroviral vectors, methods of making serum resistant retroviral vectors using the Mpf cell line, and retroviral vector producer Mpf cells. Applicants also claim using the mink cell line Mv-1-Lu for assaying the titers of retroviral vectors produced from the producer cells. The Mpf and Mv-1-Lu cell lines are essential for

practicing the claimed invention and applicants, in the instant specification, do not provide a reproducible method for generating these exact cell lines. It appears that others have deposited these cell lines at the ATCC. However, as noted in the MPEP:

The fact that applicants and other members of the public were able to obtain the material in question from a given depository prior to and after the filing date of the application in issue did not establish that upon issuance of a patent on the application that such material would continue to be accessible to the public. The applicants did not make of record any of the facts and circumstances surrounding their access to the material in issue from the depository, nor was there any evidence as to the depository's policy regarding the materials if a patent would have been granted. Further, there was no assurance that the depository would have allowed unlimited access to the material if the application had matured into a patent.

and also

The mere reference to a deposit or the biological material itself in any document or publication does not necessarily mean that the deposited biological material is readily available.

(MPEP 2404.01 and also see *Ex parte Humphreys*, 24 USPQ2d 1255 (Bd. Pat. App. & Inter. 1992)). Therefore, to ensure availability to the public for the life of any patent granted on the instant application, applicants must deposit these cells and comply with the requirements of 37 CFR 1.801-1.809.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5, 14, 15, 42 and 44 are rejected under 35 U.S.C. 112, second paragraph, as being

indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 is vague in that it depends from claim canceled claim 2.

Claim 15 is vague in that it depends from canceled claim 12.

Claim 42 and 44 (and dependent claims) are vague in that applicants recite "..said cell line is **an** (emphasis added) Mpf cell line.". Use of the word "an" implies that there is more than one Mpf cell line and it is unclear precisely what specific Mpf cell lines applicants are referring to or what properties said cell lines possess.

Claim 3 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 3 repeats the limitation that the cell line is human serum resistant.

Miscellaneous: In Claim 6, line 2, "cells" should be "cell".

Claims 1, 46 and 38 are allowed.

Claims 6, 8-9, 11, 13, 16-18, 51, 53-54, 56, 58, 61-64 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo whose telephone number is (703) 308-1906. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate .

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Faxes may be sent directly to the examiner at (703) 746-5061.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

David Guzo
February 22, 2003

DAVID GUZO
PRIMARY EXAMINER